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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/476,798	06/07/95	DEBOER H	16994-003125

020350 HM31/1119
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EXAMINER	
HAUDA,K	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/19/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/476,798	Applicant(s) Deboer et al.
	Examiner Karen M. Hauda	Group Art Unit 1632

☒ Responsive to communication(s) filed on *Sep 25, 1998* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *114-117* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *114-117* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Transitional After Final Practice

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on September 25, 1998 has been entered.

Claim Rejections - 35 USC § 102

The prior rejection of claim 98 under 35 USC § 102 is withdrawn in view of applicant's cancellation of this claim in the amendment filed September 25, 1998, paper # 22.

New Grounds of Rejection

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. 5,741,957. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed invention encompasses the transgenic bovine claimed in US Patent No. 5,741,957 and the method of making a polypeptide of interest using the transgenic bovine.

Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-28 of U.S. Patent No. 5,633,076. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed invention is an obvious variation of the method of making the transgenic bovine claimed in US Patent No. 5,633,076 and the method of making a polypeptide of interest using the same transgenic bovine. Note the phenotype of the transgenic bovine is production of protein in the milk.

Claim Rejections - 35 USC § 112

Claim 114 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 114 recites a chimeric bovine. Applicants specification fails to describe the production of a chimeric bovine, and fails to use the term "chimeric" in the specification. Should the Examiner be mistaken regarding the absence of support for the newly introduced term "chimeric" applicant is invited to point out the location of support for "chimeric" by page and line number.

Claims 114-117 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic bovine whose somatic and germ cells contain a transgene, wherein the transgene comprises in operable association a mammary gland specific promoter; a mammary gland specific enhancer; a DNA sequence encoding a signal sequence functional in bovine mammary gland secretory cells; and A DNA sequence encoding a heterologous polypeptide of interest; wherein the transgenic bovine expresses the transgene in mammary secretory cells such that the polypeptide of interest is detectable in milk produced by the transgenic bovine or a female descendent of the transgenic bovine, does not reasonably provide enablement for a chimeric bovine comprising the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 114 is directed to a transgenic or chimeric bovine. Claims 115-117 are directed to methods of producing a polypeptide using the transgenic bovine or a female descendent of claim 114. It is initially noted that Patent No 5,741,957 claiming a transgenic bovine and methods of

making a protein using said transgenic bovine has issue. It is further noted that numerous Declarations under 37 C.F.R. § 1.132 in support of enablement were made of record in application 08/461,333. It is requested that a copy of these Declarations be made of record in the instant application for completeness.

With respect to claim 114, as noted above, the term chimeric bovine is not supported in the specification. Given that chimeric bovine is not defined in the specification, it is unclear exactly how applicant's are interpreting the term chimeric, especially when the claim is read in light of the teachings in the specification directed to making transgenic bovine. Human Genetics, by Elof Axel Carlson defines chimera as, "A composite individual formed from two cell lines of separate origin." Given this definition, a chimeric bovine can be produced using transgenic technology only if embryonic stem (ES) cells are isolated. Using the technology outlined in applicants specification chimeric bovine would not be produced because any production of cells in the bovine would be from a cell of single origin- the zygote. Applicants specification fails to provide any guidance to the skilled artisan on what methodologies could be used to generate a chimeric bovine which expresses a heterologous protein in the milk of said bovine at levels which can be isolated. Furthermore, there is no evidence in the specification that applicants have isolated bovine ES cells. Applicants specification fails to teach the skilled artisan any parameters directed to this embodiment of the claimed invention.

While applicants specification describe the production of a single mosaic bovine (see pages 90 and 119 of the specification), this also is not a chimeric bovine. Human Genetics, by Elof Axel

Carlson defines mosaic as, "An individual with two strains of cells derived by nondisjunction or mutation after the zygote forms." Thus, a mosaic bovine would be a bovine where the zygote mutates to form two cells with different genetic makeup which are derived from the same cell. Since a chimera must be an individual formed from two cells of different genomic origin, these terms are not synonymous. Even assuming, arguendo, that applicants intended to claim a mosaic bovine rather than a chimeric bovine, the specification is not enabled for this aspect of an invention either. Since mosaic bovine are a result of an unexplained mutation, there is no reproducibility in generating a mosaic bovine which can produce functional protein in its milk. The phenotype of any mosaic mammal is completely unpredictable and may never be repeated because it is produced by a random mutation of a zygote. The transgenic bovine of the claimed invention are useful for producing proteins in the milk of female bovines for mass production of functional proteins. There is no support in the specification or the prior art that mosaic bovines can be produced which produce functional protein in the milk of the female bovine at a level which can be isolated without undue experimentation.

Finally, it is noted that neither mosaic bovine or chimeric bovine, by definition, pass a transgene to descendants. Applicants specification fails to describe how this can be accomplished. In fact, at page 90-91 applicants indicate that the mosaic bovine (calf #15) did not contain the transgene in its germline DNA. (As an aside, it is noted that at page 90, calf #15 is noted to be a female, however, at page 119, calf #15 is noted to be a male.) Thus, it is completely unclear how descendants of chimeric bovine can produce protein in their milk (see claim 114). Note also, that

claims 115-117 encompass a method of producing a polypeptide comprising recovering milk from the female descendant of a chimeric bovine. This is not enabled for the reasons stated above.

Therefore, it would have required undue experimentation for the skilled artisan to produce chimeric bovine or to practice a method of producing a polypeptide from descendants of the same, due to the absence of teachings in the specification, the lack of working examples provided in the specification, the state of the prior art with respect to chimeric bovine, the unpredictability to producing chimeric bovine which express functional polypeptides in milk, the nature of the invention and the breadth of the claims.

Claims 114-117 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 114 is confusing because the claim recites a "transgenic or chimeric bovine whose mammary gland cells contain a transgene" and then later recites "female descendant[s] of the transgenic or chimeric bovine". Transgenic (by definition of the art) must contain the transgene in germline cells, whereas chimeric does not have germline transmission of a transgene. However, the claim recites both somatic and germline transmission. For example, mammary gland cells would be somatic transmission, but expression in female descendants would require germline transmission. The claim is confusing based on what parameters are to refer to what, especially

given that neither "transgenic" or "chimeric" are defined in the specification. Note, claims 115-117 depend from claim 114.

Claim 115 is also indefinite because it recites "...recovering milk from the transgenic bovine or female descendant of claim 114". It is unclear if this phrase is only referring to female descendants of transgenic bovine of claim 114, or also referring to female descendants of chimeric bovine of claim 114. Clarification is necessary.

Claims 114-117 are free of the prior art of record because the prior art does not teach transgenic or chimeric bovine.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen M. Hauda whose telephone number is (703) 305-6608.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian R. Stanton, may be reached at (703) 308-2035.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-2801.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1632.

Papers related to this application may be submitted to Group 160 by facsimile transmission. Papers should be faxed to Group 160 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is or (703) 305-3014 or (703) 308-4242.

Karen M. Hauda

Karen M. Hauda
Patent Examiner
November 17, 1998